2-Cyanomethyl-1,1,3,3-tetracyanopropene, a Self-Condensation Product of Malononitrile

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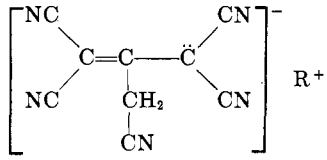
Self-condensation of malononitrile in 1 *M* sodium carbonate results in a compound (λ_{max} 358 mμ) shown to be 2-cyanomethyl-1,1,3,3-tetracyanopropene (I) which was isolated as salts. Evidence for the formation of I through the biologically interesting 2-amino-1,1,3-tricyanopropene (II) is presented and a mechanism for the formation of the former is proposed. Compound I was found to be a strong acid. The properties of I and its salts are discussed.

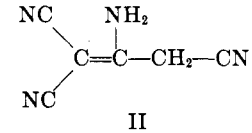
The interesting biological properties of self-condensation products of malononitrile, especially the dimer, 2-amino-1,1,3-tricyanopropene[1] (II), have been the subject of several recent publications.[2] This paper is concerned with such a product, 2-cyanomethyl-1,1,3,3-tetracyanopropene (I), and its salts (Ia–d).[3]

The presence of material in alkaline solutions of malononitrile having an absorption maximum in neutral or acidic solution at 358 mμ (shoulder between 348 and 352 mμ) was reported[4] in 1954, and the same phenomenon was later observed in these laboratories.[2a] In this paper we report the isolation of the compound responsible for this chromophore as sodium and tetraalkylammonium salts, provide evidence that the structure of the compound and its salts is represented by expression I,[5] and describe a convenient method for preparing the salts. Also of interest is a procedure that we used to determine the equivalent weight by n.m.r. spectroscopy of the tetramethylammonium salt which utilizes the built-in reference standard provided by the four methyl groups of the tetramethylammonium cation.



I, R = H
Ia, R = Na
Ib, R = $(CH_3)_4N$
Ic, R = $(CH_3CH_2)_4N$
Id, R = $(CH_3CH_2CH_2)_4N$

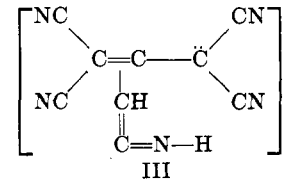
We found the residues[6] remaining after the preparation of 2-amino-1,1,3-tricyanopropene (II) by dimerization of malononitrile in methanol containing sodium methoxide, to be a rich source of material with a maximum at 358 mμ. It was from such residues that we first isolated the sodium salt (Ia) by direct crystallization from ethanol. The sodium salt is readily converted to the tetraalkylammonium salts (Ib–d).



II

Elemental analyses[7] of the salts were in accord with the empirical formula $C_9H_2N_5$ for the anion. Potentiometric titration of the acid,[8] freshly generated from the tetramethylammonium salt over a column of IR-120 (H^+) resin, gave an equivalent weight of 245 for the salt and revealed the strong acidity ($pK_a < 2.5$) of the free acid.[9] The equivalent weight determined by n.m.r. spectroscopy (see Experimental) was 242 (± 24).

The infrared spectra of the salts, determined both in Nujol mull and in chloroform solution, had the following significant bands (range of position indicated): 2270–2250 (weak, unconjugated nitrile), 2205–2190 (strong, conjugated nitrile), 1485–1500 cm.$^{-1}$ (strong, resonating double bond). A series of very weak bands, somewhat more pronounced in chloroform solution, was discernible in the region between 3580 and 3220 cm.$^{-1}$. The latter may be attributable to tautomeric ketenimino structures such as III.



III

The n.m.r. spectra of the salts in deuterated dimethylformamide have, in addition to the expected signals due to tetraalkylammonium ion, a singlet (2 protons) at δ 3.68 (referred to tetramethylsilane as internal standard). The spectra taken in deuterium oxide revealed that these two protons are fully exchangeable with the solvent.

The salts are conveniently prepared by allowing a 1.5 *M* solution of malononitrile in 1 *M* sodium carbonate to remain at room temperature for several

(1) For a convenient preparation of this compound, see E. C. Taylor and K. S. Hartke, *J. Am. Chem. Soc.*, **81**, 2452 (1959); see also R. A. Carboni, D. D. Coffman, and E. G. Howard, *ibid.*, **80**, 2838 (1958).

(2) For example, (a) F. S. Eberts, Jr., G. Slomp, and J. L. Johnson, *Arch. Biochem. Biophys.*, **95**, 305 (1961); (b) F. S. Eberts, Jr.; *Biochem. Pharm.*, **8**, 367 (1961); (c) P. W. O'Connell and F. S. Eberts, Jr., *ibid.*, **8**, 337 (1961); (d) J. Jacob and J. L. Sirlin, *Science*, **144**, 1011 (1964); (e) W. Dingman and M. B. Sporn, *ibid.*, **144**, 26 (1964).

(3) Several analogs of I in which the cyanomethyl group is substituted with a variety of substituents have been described by W. J. Middleton, E. L. Little, D. D. Coffman, and V. A. Engelhardt [*J. Am. Chem. Soc.*, **80**, 2795 (1958)]. These analogs were prepared from tetracyanoethylene.

(4) J. Mendelson, J. H. Mendelson, J. B. Fox, and R. F. Grenell, *Science*, **120**, 266 (1954).

(5) For convenience the anion is represented as in I. However, it no doubt exists as a highly resonating ion with possible contributions from several tautomeric forms.

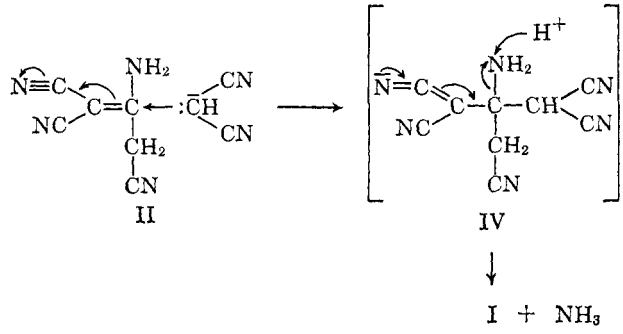
(6) We thank the Aldrich Chemical Co., Milwaukee, Wis., for providing residues.

(7) Special precautions were necessary to obtain consistent results. The best results were obtained by combustion in the presence of a tungstic oxide catalyst using a large burner.

(8) The free acid was not obtained in crystalline form.

(9) The curve was typical of that obtained by titration of a strong acid with a strong base. There was a suggestion of a second function at pK_a *ca.* 10, probably due to the titration of a second proton. This would be in accord with the ultraviolet spectrum taken in alkali. The strong acidity of I is not surprising [see R. H. Boyd, *J. Phys. Chem.*, **67**, 737 (1963)].

hours. The acidified reaction solution is then extracted with ethyl acetate and the extracted acid is converted to the desired salt. In the very early stages of the preparation the predominant chromophore (λ_{max} 272 mμ) detectable in the acidified reaction solution is identical with that of 2-amino-1,1,3-tricyanopropene (II). This chromophore soon diminishes to be replaced by a chromophore of increasing intensity having a maximum at 358 mμ (Figure 1). The latter is attributable to I. This behavior, in conjunction with the above data, led us to the conclusion that I is formed by the interaction of II with the anion of malononitrile by the substitution mechanism II → IV →:I[10] and that the structure of the product is in fact represented by I.



Our conclusion was supported by the demonstrations that 1 mole of ammonia is liberated for each mole of I produced and that, under the same conditions, I is produced from II in good yield, also with the liberation of 1 mole of ammonia.

Structures I through Id are in accord with the data presented above including the equivalence and the ready exchangeability of the two protons of the anion. Furthermore, the strong acidity of I is understandable in terms of stabilization of the anion by mesomerism.

Experimental

N.m.r. spectra were determined using a Varian Model A-60 instrument. Integrated areas were measured with a digital voltmeter.

Tetrapropylammonium Salt of 2-Cyanomethyl-1,1,3,3-tetracyanopropene (Id) from Malononitrile.[11]—A solution of 10 g. of freshly distilled malononitrile in 100 ml. of 1 *M* sodium carbonate was allowed to remain at room temperature for 19 hr. The solution was then acidified with 20 ml. of concentrated hydrochloric acid (acidic to congo red) and extracted with three 75-ml. portions of ethyl acetate. The extracts were washed with three 30-ml. portions of 0.1 *N* hydrochloric acid, combined, and evaporated *in vacuo*. The residue was dissolved in 50 ml. of water, and the solution was adjusted to pH 6.8 with 40% sodium hydroxide and treated with 11.5 g. of tetrapropylammonium bromide dissolved in 100 ml. of water. The salt, which crystallized immediately, weighed (after drying) 15.3 g. (83% yield) and melted at 94°. After crystallization from methanol–water the melting point was 95°; λ_{max}^{EtOH} 358 mμ (ϵ 31,000) and 348–352 mμ (sh) (ϵ 29,000); $\lambda_{max}^{0.1\ N\ NaOH\ in\ EtOH}$ 314 mμ (ϵ 26,200) and 337 mμ (ϵ 22,700); in dilute hydrochloric acid the spectrum was the same as in neutral ethanol.

Anal. Calcd. for $C_{21}H_{30}N_6$: C, 68.82; H, 8.25; N, 22.93. Found: C, 69.08; H, 8.24; N, 23.18.

Sodium Salt of 2-Cyanomethyl-1,1,3,3-tetracyanopropene (Ia) from Malononitrile.—A solution of 100 g. of malononitrile in 1 l. of 1 *M* sodium carbonate was allowed to remain at room temperature for 17 hr. The solution was then acidified (to congo red) with 170 ml. of concentrated hydrochloric acid and extracted with four 250-ml. portions of ethyl acetate. Anhydrous sodium bicarbonate (85 g.) was added to the combined extracts, and the mixture was stirred for 2 hr. The mixture was filtered, and the solid was washed with two 250-ml. portions of a mixture of ethyl acetate and chloroform (60% ethyl acetate). The combined filtrate and washings were diluted with 800 ml. of chloroform to precipitate an oil which crystallized. After drying, the collected crystals weighed 68 g. (66%); judged by the ultraviolet spectrum, the product was at least 90% pure. Recrystallized from ethanol, it melted at 248–250° dec.; ultraviolet spectrum identical with that of Id.

Anal. Calcd. for $C_9H_2N_5Na$: C, 53.20; N, 34.48; Na, 11.32. Found: C, 53.14; N, 34.56; Na, 11.12.

Tetramethylammonium Salt of 2-Cyanomethyl-1,1,3,3-tetracyanopropene (Ib).—A solution of 2.03 g. of the sodium salt (Ia) in 30 ml. of water was applied to a column (1.8-cm. diameter) of 50 ml. of IR-120 (H^+) resin. The column was eluted with water while the effluent was titrated with 1 *N* tetramethylammonium hydroxide at such a rate as to keep the pH at approximately 7.0. After 75 ml. of effluent had been collected, no more acidic material could be eluted. The effluent was lyophilized and the residue, after crystallization from absolute ethanol, yielded 1.83 g. (72%) of the crystalline salt, m.p. 104°; the ultraviolet spectrum was identical with that of Id.

Anal. Calcd. for $C_{13}H_{14}N_6$: C, 61.40; H, 5.55; N, 33.05. Found: C, 61.31; H, 5.15; N, 32.88.

Tetraethylammonium Salt of 2-Cyanomethyl-1,1,3,3-tetracyanopropene (Ic).—A solution of 1.624 g. of the sodium salt (Ia) in 10 ml. of water was added to a solution of 1.82 g. of tetraethylammonium bromide in 7 ml. of water. The precipitate, which formed immediately, yielded 1.90 g. (77%) of the crystalline salt on crystallization from methanol–water. It had a melting point of 85°; ultraviolet spectrum identical with that of Id.

Anal. Calcd. for $C_{17}H_{22}N_6$: C, 65.78; H, 7.14; N, 27.08. Found: C, 65.81; H, 7.41; N, 27.23.

Tetrapropylammonium Salt of 2-Cyanomethyl-1,1,3,3-tetracyanopropene (Id) from Sodium Salt (Ia).—A solution of 1.624 g. of the sodium salt in 10 ml. of water was added to a solution of 2.24 g. of tetrapropylammonium bromide in 10 ml. of water. The precipitate, which formed immediately, yielded 2.30 g. (78%) of the salt Id, identical with the sample described in the first experiment.

Titration of Acid (I) from the Tetramethylammonium Salt (Ic). The tetramethylammonium salt (53.13 mg.) was applied, in a few milliliters of water, to a column (7-mm. diameter) containing 5 ml. of IR-120 (H^+) resin. The column was eluted (*ca.* 1 ml./min.) with water and the effluent (20 ml.) was titrated potentiometrically with standard 0.1 *N* sodium hydroxide. The titration curve was typical of that obtained by titration of a strong acid with a strong base. From the curve the following data were determined: equiv. wt. (for the salt), 245; pK_a of the free acid, less than 2.5 (slight inflection at pK_a *ca.* 10).

Molecular Weight of the Tetramethylammonium Salt (Ib) by N.m.r.—The instrument response, 1.2 ± 0.2 v./mequiv. of H,

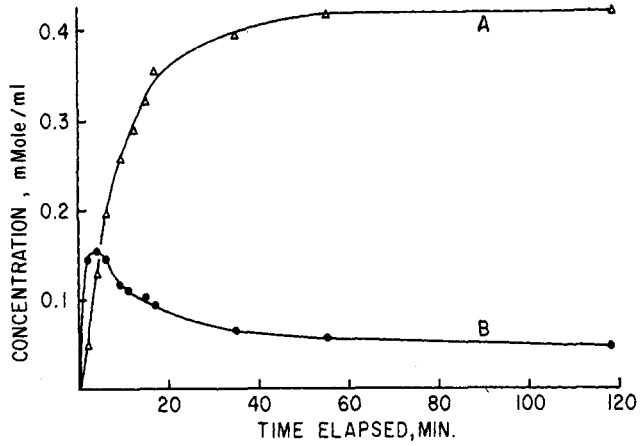


Figure 1.—Composition of reaction solution during the preparation of I by self-condensation of malononitrile in carbonate solution. Curve A refers to I and curve B to II. The curves were plotted from data presented in Table I.

(10) For a similar type of reaction, see A. D. Josey, *J. Org. Chem.*, **29**, 707 (1964).

(11) For a preparation of this salt from the sodium salt see below.

was determined using a deuterium oxide solution of acetonitrile as standard (0.66 ml. of solution containing 30.4 mg. of acetonitrile). A solution of the salt in deuterium oxide (0.66 ml. of solution containing 74.5 mg. of salt) resulted in a singlet of 0.9 ± 0.0 v. due to exchangeable hydrogen and another singlet of 4.5 ± 0.1 v. due to N-methyl. This represents 0.58 ± 0.05 mequiv. of exchangeable hydrogen and 3.7 ± 0.4 mequiv. of hydrogen due to N-methyl. Since the singlet due to N-methyl contains 12 hydrogens, the calculated molecular weight is 242 ± 24 (assuming a monotetramethylammonium salt) and there are 1.9 ± 0.2 exchangeable hydrogens/molecule.

Determination of Ammonia Produced during the Preparation of I from Malononitrile.—A solution of 25.0 g. of freshly distilled malononitrile in 250 ml. of 1 *M* sodium carbonate was allowed to remain at room temperature for 19 hr. A 1-ml. aliquot of the reaction solution was dilu tedwith 2 ml. of 1 *N* hydrochloric acid and further diluted, by a factor of 100, with 0.1 *N* hydrochloric acid for a spectral analysis which showed the concentration of I in the reaction solution to be 0.44 mmole/ml. (87% yield). A 100-ml. portion of the reaction solution was acidified with 20 ml. of concentrated hydrochloric acid and extracted with three 75-ml. portions of ethyl acetate and finally with 75 ml. of ether. The organic extracts were washed with three 30-ml. portions of 0.1 *N* hydrochloric acid. By the procedure described in the first experiment, the tetrapropylammonium salt was isolated from the combined organic extracts in 83% yield (94% of the yield calculated above). The combined acidic aqueous layers were diluted to 250 ml. with water. A 5-ml. aliquot of this solution was treated with 10 ml. of 4 *N* sodium hydroxide and heated on the steam bath while a stream of purified nitrogen was passed through it into 25 ml. of 2% boric acid. The volatile base, collected in the buffer solution, was titrated with standard 0.1 *N* hydrochloric acid using a mixed methylene blue–methyl red indicator. After 165 min., the total volatile base titrated was 0.89 mequiv. Assuming the volatile base to be entirely ammonia (see below) this represents an 86% yield (99% of the yield expected from spectral analysis). In a parallel experiment, the volatile base was trapped in 25 ml. of 0.1 *N* hydrochloric acid. The acidic solution, on treatment with 250 mg. of *p*-(*p*-hydroxyphenylazo)benzenesulfonic acid, yielded 225 mg. of derivative identical with the authentic derivative of ammonia (melting point, mixture melting point, and infrared spectrum). This represents 85% of the titrated volatile base.

Preparation of I from 2-Amino-1,1,3-tricyanopropene (II) and Determination of Ammonia Produced.—A solution of 3.30 g. of II and 1.65 g. of freshly distilled malononitrile in 50 ml. of 1 *M* sodium carbonate was left at room temperature for 19 hr. The following results were obtained on analysis of the reaction solution by the procedures described in the preceding experiment: (a) the concentration of I in the reaction solution was found to be 0.43 mmole/ml. (86% yield) by spectral analysis, and of this 92% was isolated as the tetrapropylammonium salt; (b) the yield of volatile base by titration was 89% of that expected from spectral analysis of which 82% was isolated as the *p*-(*p*-hydroxyphenylazo)benzenesulfonic acid salt of ammonia.

Spectral Analysis of the Reaction Solution during the Preparation of I from Malononitrile.—A solution of 5.050 g. of freshly distilled malononitrile in 50 ml. of 1 *M* sodium carbonate was allowed to remain at room temperature. At intervals, 1 ml. of the solution was diluted to 100 ml. with 0.1 *N* hydrochloric acid (reaction quenched) for determination of the ultraviolet spectrum. The concentration of I in the reaction solution was calculated from the maximum at 358 mμ using ε 30,500; the concentration of 2-amino-1,1,3-tricyanopropene (II) was similarly calculated from the maximum at 272 mμ using ε 15,500. The initial concentration of malononitrile was 1.53 mmoles/ml. The results are summarized in Table I (see also Figure 1).

TABLE I

ANALYSIS OF REACTION SOLUTION DURING PREPARATION OF I

Elapsed time, min.	—Calcd. concn., mmole/ml.— II	I
2	0.145	0.048
4	0.154	0.128
6	0.148	0.197
9	0.116	0.256
12	0.112	0.289
15	0.103	0.322
17	0.095	0.354
34	0.067	0.394
56	0.057	0.417
118	0.046	0.420

Acknowledgment.—We thank Dr. G. Umbriet and associates and F. A. MacKellar of these laboratories for elemental analyses and determination of n.m.r. spectra.

Synthesis of Some 1-Substituted 2,2-Dimethyl-3-isopropylidenecyclopropanes[1a]

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Synthetic routes to compounds with general structure **3** have been examined in the hope of developing a synthesis of **1**, the reported structure for the sex attractant of *Periplaneta americana*. The Bamford–Stevens ring contraction of **9** gave the isopropylidenecyclopropane **10**, but the corresponding tosylhydrazone **6** gave a very complex mixture of products. Diazoacetic ester addition and dibromocarbene addition to tetramethylallene provide access to a variety of 1-substituted 2,2-dimethyl-3-isopropylidenecyclopropanes, whose spectral properties are at variance with those reported for **1**. Several reactions of these compounds are reported, of which the most interesting is the transformation of the allylic cyclopropyl bromide **24** to the allenic ester **25** on treatment with silver propionate.

The report of the isolation of a sex attractant from the virgin female American cockroach, *Periplaneta americana* L., and of its identification as 2,2-dimethyl-3-isopropylidenecyclopropyl propionate (**1**)[2] has aroused unusual interest.[3] The estimate that less than 30 molecules (~10^{-20} g.) of this substance is needed to elicit a response in male roaches characterizes it as one of the physiologically most active substances ever described.[4] Although the postulated structure has a superficial similarity to that of pyrethrin I (**2**), a highly

(1) (a) The partial support of this research by the National Institutes of Health (Grant Numbers 5-TI GM-834-03 and E 2908) is gratefully acknowledged. (b) National Science Foundation Postdoctoral Fellow, 1962–1963. (c) National Science Foundation Undergraduate Research Participant, 1963. (d) National Institutes of Health Postdoctoral Fellow, 1963–1964.

(2) M. Jacobson, M. Beroza, and R. T. Yamamoto, *Science*, **139**, 48 (1963).

(3) *Time*, (Jan. 18, 1963); *Washington Post* (Aug. 18, 1963); *Science*, **140**, 1367 (1963); *Sci. Am.*, **211**, 20 (1964); *New York Times* (Aug. 18, 1963); *Chem. Eng. News*, **41**, 126 (1963).

(4) H. S. Mosher, F. A. Fuhrman, H. D. Buchwald, and H. G. Fischer, *Science*, **144**, 1103 (1964).